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Review

Biophysical methods: Complementary tools to study the influence of human steroid hormones on the liposome membrane properties

Rola Abboud [a, b], Catherine Charcosset [b], Hélène Greige-Gerges [a, *]

[a] Bioactive Molecules Research Laboratory, Faculty of Sciences, Lebanese University, Lebanon
[b] Laboratoire d'Automatique et de Génie des Procédés (LAGEP), UMR-CNRS 5007, Université Claude Bernard Lyon 1, CPE Lyon, Bat 308G, 43 Boulevard du 11 Novembre 1918, F-69622 Villeurbanne Cedex, France

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ABSTRACT

Human steroid hormones are involved in many aspects of physiology and have long been known to exert rapid and delayed effects. They are lipophilic molecules which can be incorporated into the lipid membranes. Through non-covalent interactions they can alter the properties of the membrane, including fluidity, lipid raft formation and others. In this review, different biophysical techniques were described to study the interaction of human steroid hormones with biological and biomimetic membranes such as differential scanning calorimetry, electron paramagnetic resonance, fluorescence spectroscopy and Fourier transform infrared spectroscopy. The aim of this review is to overview the results of these complementary biophysical techniques summarizing the effects of these hormones on thermotropic and dynamic membrane properties. Meanwhile, the disorder induced by human steroid hormones is discussed in terms of hydrophobicity and chemical structure.

Contents

Abbreviations: ANS, 1-anilino-8-naphthalene sulfonate; 12-AS, 12-(9-antroiloxy)-stearic acid; BDP, beclomethasone dipropionate; BM, betamethasone; Co, cortisol; Cpa, cyproterone acetate; DEX, dexamethasone; DSC, differential scanning calorimetry; DHT, dihydrotestosterone; DMPC, 1,2-dimyristoyl-*sn*-glycero-3-phosphocholine; DPPC, dipalmitoylphosphatidylcholine; DPH, 1,6-diphenyl-1,3-5-hexatriene; DSPC, 1,2-distearoyl-*sn*-glycero-3-phosphocholine; DYG, dydrogesterone; EPR, electron paramagnetic resonance; E_2, 17β-estradiol; E_3, estriol; 9-FA, 9-fluorocortisol acetate; FTIR, Fourier transform infrared spectroscopy; 17-OHPG, 17-hydroxyprogesterone; 21-OHPG, 21-hydroxyprogesterone; MP, medroxyprogesterone; MPA, medroxyprogesterone acetate; MPd, methylprednisolone; PC, phosphatidylcholine; Pd, prednisolone; Pdn, pregnanedione; PG, progesterone; SR, sarcoplamsic reticulum; SAM, sperm acrosomal membrane; SPM, sperm plasma membrane; SyPM, synaptosomal plasma membrane; TMA-DPH, 4-trimethyl-ammonio-1,6- diphenyl-1,3,5-hexatriene.

* Corresponding author. Faculty of Sciences, Section II, Lebanese University, B.P. 90656 Jdaidet el-Matn, Lebanon.
E-mail addresses: hgreige@ul.edu.lb, greigegeorges@yahoo.com (H. Greige-Gerges).

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1. Introduction

Human steroid hormones represent a large class of biologically active molecules. Their classical genomic mechanism of action involves their binding to nuclear and specific intracellular receptors, which act as ligand-dependent transcription factors exerting different effects on the expression of target genes. Same for the delayed genomic action, increasing evidence for rapid, non-genomic steroids effect has been demonstrated for virtually all groups of steroids [1–5]. Steroids represent three non-genomic mechanisms of action: i-steroids have a membrane-bound receptors and are associated with adenylyl cyclase, also termed adenylate cyclase, and second messenger cascades [6–9]; ii-steroids also have a specific binding site on neurotransmitter receptors [10,11]; iii- or they can intercalate into the lipid membranes resulting in the perturbation of lipid-lipid interactions thus modulating cell functions [12,13].

Steroid hormones are all synthesized from cholesterol and show structural similarities [14]. Fig. 1 summarizes the biosynthetic pathways of the major steroid hormones [15,16]. These latter regulate a wide variety of developmental and physiological processes from fetal life to adulthood [14,17]. Among these many processes are conception, intrauterine fetal development, bone maturation, immune system regulation, water and electrolyte homeostasis, central nervous system activity and others [17]. There are five major classes of human steroid hormones: androgens, estrogens, progestogens, glucocorticoids and mineralocorticoids [14].

Biological membranes play an important role in the cellular protection, in addition to controlling the transport of nutrients. They present a complex composition of lipids and proteins. The lipid part contains a variety of head group and acyl chain structures, sphingolipids and sterols [18]. The existence of long and saturated acyl chains in lipids allows cholesterol to be closely packed in the lipid bilayer, resulting in the organization of liquid-ordered (l_o) phases [19]. Sphingolipids, sterols and saturated acyl chains can cluster to form microdomains called rafts [20] that exist in the liquid ordered phase (l_o) and are detergent-insoluble membrane domains [21,22]. Raft formation is coupled to the packing and ordering of the molecules in the bilayer [23]. The functions of rafts are reported in literature [20,24–26]. Since biological membranes are considered complex, simpler biomimetic model membranes have been developed. The most common cell membrane models range from vesicles to different types of supported lipid bilayers, although lipid monolayers have also been studied [27].

The interaction of steroids with polar head groups and non-polar hydrocarbons chains of lipid membranes, or both, can induce several changes in the membranes functions such permeability, lipid rafts formation and fluidity. The steroids effect on domain formation is studied extensively in literature [21,28,29]. The documented activities of steroids was translated into quantitative data by Wenz [30] where steroids were divided into two categories: i-promoters, which are steroids of rigidifying, molecular ordering, condensing effect, and/or raft promoting/stabilizing ability on membranes, ii-disrupters, which are steroids of fluidifying, disordering, and/or raft disrupting/destabilizing effect on membranes [30].

Among steroids, human steroid hormones were selected in this review to summarize their effect on liposome membrane fluidity, since liposomes are the most common biomimicking models largely used for investigating drug-membrane interactions. Fig. 2 represents the chemical structures of steroid hormones that appear throughout the review. The main techniques used to study human steroid membrane interaction are introduced, and literature data are resumed into conclusive tables. Finally, a conclusion is prepared to give an overview on the effect of human steroid hormones on membrane fluidity and the role of their hydrophobicity and functional groups in the steroid membrane interaction.

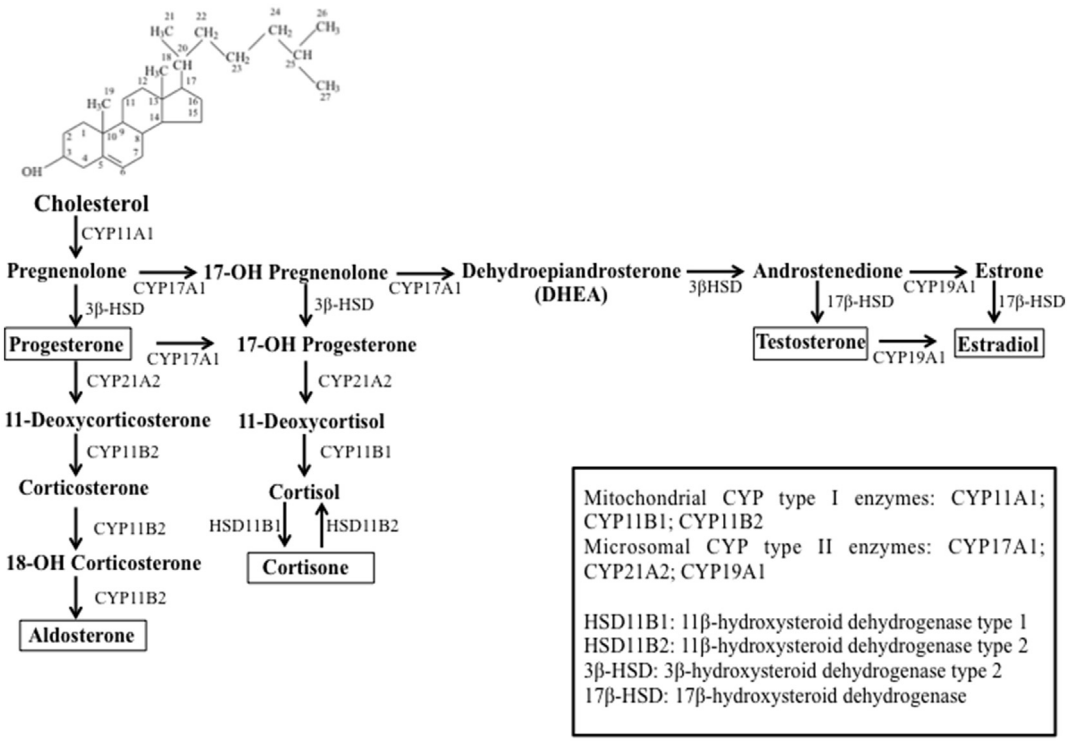

Fig. 1. Steroid hormones biosynthetic pathways.

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